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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/705,618	11/10/2003	Lynn E. Spitler	204372000902	4690

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EXAMINER	
HUMPHREY, DAVID HAROLD	
ART UNIT	**PAPER NUMBER**
1643	

DATE MAILED: 08/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/705,618	SPITLER ET AL.	
	Examiner	Art Unit	
	David Humphrey	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 May 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *54-74* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *54-71* is/are rejected.

7)☒ Claim(s) *72-74* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *05/25/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendments and Arguments

1. The Office acknowledges the receipt of Applicants' amendment to the claims in the response filed on 25 May 2006. Claims 63-74 are added.

Claims 54-74 are pending.

Claims 54, 57, and 60 are amended.

Claims 54-74 are examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

New Grounds of Objection

3. Claims 72, 73, and 74, are objected to for depending on rejected claims.

Maintained Rejections

Claim Rejections - 35 USC § 112, first paragraph

4. The rejection of claims 54-62 and newly added claims 63-71, under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating a subject by administration of an anticancer agent, CPT-11, and JBT3002 in multilamellar vesicles to reduce intestinal damage (intestinal mucositis) does not reasonably provide enablement for a method of treating a subject with any

anti-neoplastic agent and JBT3002 to alleviate intestinal damage (intestinal mucositis) is maintained and made. Further, the specification is not enabling for "prevention" of mucositis.

The claims are directed to a method of alleviating or preventing intestinal mucositis in a subject associated with treatment with an anti-neoplastic agent. The claimed method requires the administration of JBT3002 (N-palmitoyl-S-[2(R,S), 3-dilauroyloxy-propyl]-(R)-cysteine) in an amount sufficient to alleviate or prevent said side effect. The claims also recite encapsulating JBT 3002 in liposomes and more specifically multilamellar liposomes.

Applicants argue that the specification is enabling for "prevention" of side effects since Example 14, on pages 60-62, states that treatment with JBT 3002 was followed by treatment with CPT-11, see Remarks, page 7, first full paragraph, lines 3-5. Applicants further point out that in the discussion summarizing the results, it is clearly stated that the treatment of JBT 3002 followed by CPT-11 prevents disruption of the intestinal architecture as demonstrated through hematoxylin and eosin (H&E) staining of the pathology samples, see Remarks, page 7, first full paragraph, lines 5-7. Applicants also direct the Examiner to Figure 21 and page 51 which demonstrate that intestinal architecture in mice pretreated with JBT 3002 is remarkably well preserved, see Remarks, page 9, second full paragraph, lines 1-5.

With respect to oral and esophageal mucositis, Applicants submit that demonstrating reduction of intestinal mucositis is sufficient since it is well known in the art that oral mucosa, esophageal mucosa, and gastrointestinal mucosa share a

common embryologic origin, see Remarks, page 9, third full paragraph, lines 1-3. Applicants further argue that it has been long known in the art that chemotherapeutic drugs that cause oral ulceration typically also cause gastrointestinal ulceration, citing Cadman et al. (1991), see Remarks, page 9, third full paragraph, lines 8-13. Applicants further cite Skubitz et al. (1996) who teach that therapy for oral mucositis was based on knowledge of intestinal physiology, see Remarks, page 10, lines 4-9. Applicants argue Skubitz et al. teach on page 225 that the fact that glutamine supplementation was effective for oral mucositis in addition to intestinal mucositis, strongly suggested that the two conditions share a common mechanism, see Remarks, page 10, lines 10-12.

Applicants argue that the amended claims do not claim any anti-neoplastic agent but rather those anti-neoplastic agents that result in modified IL-15 levels in a subject, see Remarks, page 8, first paragraph, lines 3 and 4. Applicants further submit that the art cited by the Examiner, Smorenburg et al., describes the use of two or more drugs used in combination for their anti-neoplastic effects in contrast to the claimed invention which discloses a method of using JBT 3002 as an agent that prevents or alleviates a specific side effect, see Remarks, page 8, second paragraph, lines 1-5. Applicants conclude that Smorenburg et al. in fact teaches that combination drug therapy is not simple, but it is routine and well-known in the art, see Remarks, page 8, last sentence bridging page 9.

Applicants' arguments have been carefully considered but found not persuasive. First of all, it is not clear from figure 22 that intestinal mucositis has been "prevented". In fact, the H&E staining of the JBT3002/CPT11 treated ileum looks more inflamed than

does the ileum treated with CPT-11 alone. While the specification may be enabling for reducing or alleviating intestinal mucositis it is not enabled for preventing intestinal mucositis. The definition of prevent is "to keep from happening." Therefore, a higher standard is required to demonstrate that a side effect or disease, etc., has been prevented since even lessening the degree of intestinal mucositis would not be considered preventing the side effect. The specification does not provide support for claims to "preventing intestinal mucositis" as limited data is provided regarding the protective effects of JBT3002 when administered prior to CPT-11 (Example 14). Only one H&E stained mouse ileum sample is provided in Figure 22 and it is not clear from the description on page 61 how many mice were actually utilized. Therefore, due to the lack of working examples as well as the unpredictability of the art, one of ordinary skill in the art would conclude the that specification is not enabling for a method of preventing intestinal mucositis.

Contrary to Applicants' assertions, the claims recite any anti-neoplastic agent. Newly added claims 63, 66, and 69, do recite increased levels of endogenous IL-15 but that appears to be due to the effects of JBT3002 and not the anti-neoplastic agent. If the claims are amended to recite an anti-neoplastic agent that increases the level of IL-15, a rejection under 35 U.S.C. 112, first paragraph, written description, will be applied. Applicants argue that the claims do not recite any anti-neoplastic agent but those anti-neoplastic agents that result in elevated levels of IL-15. Applicants' arguments concerning Smorenburg et al. are noted. However, the Examiner cited the Smorenburg reference as evidence that one of ordinary skill cannot just combine any two anti-cancer

therapies and expect a more effective treatment. Since Applicants disclose the use of only one anti-neoplastic agent, CPT-11, in combination with JBT3002 to reduce CPT-11-induced intestinal damage of C57/BL/6 mice (see Specification page 52, Example 8 and corresponding Figure 21; page 60, Example 14, and corresponding Figure 22), undue experimentation would be required to make and use the invention commensurate in scope with the claims which encompass any anti-neoplastic agent.

No examples of prevention of oral or esophageal mucositis are presented in the specification. While the Examiner concurs that oral or esophageal mucositis may have common origins as intestinal mucositis, the specification is not enabled for preventing any type of mucositis, whether intestinal, oral, or esophageal.

Therefore, one of ordinary skill in the art would conclude that utilizing the method of treating a subject with a neoplastic agent and JBT3002 to prevent mucositis would require undue experimentation in order to practice the invention as claimed by the Applicants.

Conclusion

5. No claim is allowed.

6. Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE

MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Humphrey whose telephone number is (571) 272-5544. The examiner can normally be reached on Mon-Fri 8:30AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David Humphrey, Ph.D.

July 28, 2006

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER